

Notice of Allowability

Application No.

10/663,418

Examiner

Michael D. Burkhardt

Applicant(s)

MCCABE ET AL.

Art Unit

1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to the response to election of 3/25/2005.
2. ☒ The allowed claim(s) is/are 1-4, 7-9, 12-14.
3. ☒ The drawings filed on 15 September 2003 are accepted by the Examiner.
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) ☐ All b) ☐ Some* c) ☐ None of the:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
 - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
 - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
 - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

- | | |
|---|---|
| 1. <input type="checkbox"/> Notice of References Cited (PTO-892) | 5. <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 2. <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 6. <input checked="" type="checkbox"/> Interview Summary (PTO-413),
Paper No./Mail Date <u>5/20/2005</u> . |
| 3. <input type="checkbox"/> Information Disclosure Statements (PTO-1449 or PTO/SB/08),
Paper No./Mail Date _____ | 7. <input checked="" type="checkbox"/> Examiner's Amendment/Comment |
| 4. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit
of Biological Material | 8. <input checked="" type="checkbox"/> Examiner's Statement of Reasons for Allowance |
| | 9. <input type="checkbox"/> Other _____ |

S. O. O. 

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Daniel Reiger on 5/20/2005.

The application has been amended as follows:

In the specification:

Please delete Table 9B in the specification: page 120, line 6 to page 149, line 13.

In the claims:

1. (currently amended) An *in vitro* method of predicting the association of a test agent with zone 3 necrosis, comprising:

a) determining the level of expression of each of the genes listed in Table 5 in a cell exposed to said test agent;

b) comparing said level of expression to the level of expression of said genes in a control population exposed to at least one control agent;

c) identifying a statistically significant alteration in the level of expression of said genes in the presence of the test agent;

wherein, if present, said alteration indicates that said test agent is predicted to be associated with zone 3 necrosis ~~toxic~~.

Art Unit: 1636

3. (currently amended) An *in vitro* method of predicting the association of a test agent with zone 3 necrosis, comprising:

- a) determining the level of expression of each of the TOXMARKER 42, 59, 65, 66, 71, 76, and 97 genes in a cell exposed to said test agent;
- b) comparing said level of expression to the level of expression of said genes in a control population exposed to at least one control agent;
- c) identifying a statistically significant alteration in the level of expression of said genes in the presence of the test agent;

wherein, if present, said alteration indicates that said test agent is predicted to be associated with zone 3 necrosis ~~toxic~~.

Please cancel claims 5-6.

7. (currently amended) An *in vivo* method of predicting the association of a test agent with zone 3 necrosis, comprising:

- a) providing a cell from a subject exposed to said test agent;
- b) determining the level of expression of each of the TOXMARKER 42, 59, 65, 66, 71, 76, and 97 genes in said cell;
- c) comparing said level of expression to the level of expression of said genes in a control population exposed to at least one control agent;

Art Unit: 1636

- d) identifying a statistically significant alteration in the level of expression of said genes in the presence of the test agent;

wherein, if present, said alteration indicates that said test agent is predicted to be associated with zone 3 necrosis ~~toxic~~.

9. (currently amended) A method for screening for changes in gene expression associated with a toxic agent, comprising:

- a) determining the level of expression of each of the genes listed in Table 5 in a cell exposed to a test agent;
- b) comparing said level of expression to the level of expression of said genes in a control population exposed to at least one control agent;
- c) identifying a statistically significant alteration in the level of expression of said genes in the presence of the test agent

thereby screening for changes in gene expression associated with a toxic agent.

12. (currently amended) A method of predicting the association of a test agent with zone 3 necrosis, comprising:

- a) determining the level of expression of TOXMARKER 71 in a cell exposed to said test agent;
- b) determining the level of expression of at least one TOXMARKER selected from the group consisting of TOXMARKERS 1-70 and 72-129 ~~132~~ in said cell;
- c) comparing the level of expression in said cell of TOXMARKER 71 and the

Art Unit: 1636

TOXMARKER(s) selected in step (b) to the level of expression in a control population exposed to at least one control agent; and

d) identifying a statistically significant alteration in the level of expression of said genes in the presence of the test agent,

wherein, if present, said alteration indicates that said test agent is predicted to be associated with zone 3 necrosis ~~toxic~~.

The following is an examiner's statement of reasons for allowance: the prior art does not teach or suggest the instantly claimed method because TOXMARKER 71 (found in all the allowed claims) is novel in terms of the claimed method. Whereas other pending applications, such as 10/663,329 and 10/256,981, also claim similar methods to predict zone 3 necrosis or hepatotoxicity, neither discloses the use of TOXMARKER 71 in the methods. It should also be noted that the TOXMARKER 71 sequence was disclosed, but never made public, in prior applications 09/264,807 and 09/593, 334 (both abandoned) as a portion of a larger sequence 274 base pair sequence. Additionally, these prior applications did not disclose the instant methods, nor associate TOXMARKER 71 with zone 3 necrosis.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael D. Burkhardt whose telephone number is (571) 272-2915. The examiner can normally be reached on M-F 8AM-5PM.

Art Unit: 1636

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michael D. Burkhardt
Examiner
Art Unit 1636


DAVID GUZO
PRIMARY EXAMINER